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IMMUNE RESPONSES IN PARASITIC DISEASES.(U)
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Report Number 2

"Immune Responses in Parasitic Diseases"

Annual Summary Report

Daniel J. Stechschulte, M.D.
Herbert B. Lindsley, M.D.

1 July 1977

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U. S. ARMY MEDICAL RESEARCH AND DEVELOPMENT COMMAND
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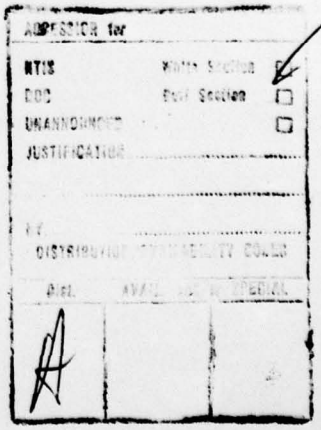

I. The generation of high-titered monospecific antisera to the rat immunoglobulins has required the continual purification of the rat immunoglobulins of the IgG1 and IgM class. The initial antisera raised to these immunoglobulins required multiple absorptions in order to produce monospecific reagents. The purification technique for the IgG1 immunoglobulin has been altered to include extraction from 7½% polyacrylamide gels, and this has resulted in the generation of a 7S molecule which is homogeneous on polyacrylamide gels which is free of contaminating proteins as assessed by immunochemical analysis utilizing antisera to rat serum. This has permitted the development of a radial immunodiffusion assay for the quantitation of total IgG1 protein in the sera of animals infected with T. rhodesiense 1886 for comparison of the change in total immunoglobulin level during the course of the infection. The purification of IgM has included the utilization of preparative starch block electrophoresis followed by G200 gel filtration. This preparation is free of the major contaminant, (α2 macroglobulin) and initial studies with serum from goats immunized with this preparation are encouraging. In addition, goats have been immunized with the immunoprecipitate obtained with goat anti-IgM reacting in agar with rat IgM.

A. The humoral immune response in rats infected with T. rhodesiense 1886 has been assessed and the following conclusions can be made: (1) hypocomplementemia develops with increasing parasitemia and both the classical pathway are involved as assessed by hemolysis assay utilizing sensitized sheep red blood cells for assessment of the classical pathway and hemolysis of rabbit red blood cells for assessment of the alternative pathway.

B. The immune response in rats infected with T. rhodesiense is characterized by the generation of antibody to both DNA and RNA consistent with observations in other species. The relationship of the autoantibody to the disease process is not known.

C. The initial results utilizing radioimmunoelectrophoresis suggested an enhancement of IgG1 and IgM antibody to an unrelated antigen such as DNP during the course of T. rhodesiense infections in the rat. Further assessment of this response utilizing radiolabeled antigen-binding for measurement of the antibody response does not confirm the results obtained with radioimmunoelectrophoresis. Thus, the marked hypergammaglobulinemia, particularly involving the gamma 1 and IgM classes, during an infection with this parasite does not extend to cells with the prior commitment to producing antibodies of a selected specificity. This would argue that the hypergammaglobulinemia represents an antibody response to parasite antigens or alternatively that only uncommitted plasma cells are capable of responding to this uncharacterized stimulus.

II. Studies have continued in collaboration with Dr. Nagle into the development of T. rhodesiense induced glomerulonephritis in the rat. Electron microscopic and immunofluroescent studies clearly indicated a glomerular lesion in this model, and studies are in progress which are designed to characterize the antibody depositing in the kidney and if possible identify an associated antigen.

III. Because of the unavailability of sufficient quantities of monospecific antisera to the various rat immunoglobulins no studies have been initiated to study and isolate protective antibody in this infection. Adoptive transfer studies with lymphocytes are also pending.

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